

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 C07K14/575 C07K14/605 A61K38/26 A61P3/10 //C12N5/06,  
 A61K47/48

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
 IPC 7 C07K A61K C07D C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, EMBASE

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 43708 A (MADSEN KJELD ; NOVONORDISK AS (DK); HUUSFELDT PER OLAF (DK); KNUDSE 2 September 1999 (1999-09-02) claim 89 ---	1-78
X	WO 01 32158 A (SQUIBB BRISTOL MYERS CO ; PIPER BETH ANNE (US)) 10 May 2001 (2001-05-10) claim 69 ---	1-78
X	US 6 358 924 B1 (HOFFMANN JAMES ARTHUR) 19 March 2002 (2002-03-19) claim 11 ---	1-78
X	WO 01 04156 A (LARSEN BJARNE DUE ; NEVE SOEREN (DK); MIKKELSEN JENS DAMSGAARD (DK)) 18 January 2001 (2001-01-18) claims 1-48 ---	1-78
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the International filing date
- "L" document which may throw doubt on priority, claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the International filing date but later than the priority date claimed

"T" later document published after the International filing date or priority date and not in conflict with the application but which may be of interest in understanding the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the International search

30 September 2003

Date of mailing of the International search report

22.10.2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340 2340, Tx. 31 651 epo nl  
Fax: (+31-70) 340 2016

Authorized officer

FERNANDO FARIETA /EÖ

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	EP 1 329 458 A (ZEALAND PHARMA AS) 23 July 2003 (2003-07-23) claim 6 ---	1-78
X	ANDREW A. YOUNG ET AL: "Studies in Obese Diabetic (ob/ob, db/db) Mice, Diabetic Fatty Zucker Rats, and Diabetic Rhesus Monkeys (Macaca mulatta)" DIABETES, vol. 48, May 1999 (1999-05), pages 1026-1034, XP002256109 figures 1,2	1-78
X	LISA JUNTTI-BERGGREN ET AL: "The Antidiabetogenic Effect of GLP-1 Is Maintained During a 7-Day Treatment Period and Improves Diabetic Dyslipoproteinemia in NIDDM Patients" DIABETES CARE, vol. 19, no. 11, November 1996 (1996-11), pages 1200-1206, XP002256110 figure 1	1-78
X	DAVID G. PARKES ET AL: "Insulinotropic Actions of Exendin-4 and Glucagon-Like Peptide-1 In Vivo and In Vitro" METABOLISM, vol. 50, no. 5, May 2001 (2001-05), pages 583-589, XP002256111 figure 2	1-78
A	RÉMY BURCELIN ET AL: "Long-Lasting Antidiabetic Effect of a Dipeptidyl Peptidase IV-Resistant Analog of Glucagon-Like Peptide-1" METABOLISM, vol. 48, no. 2, February 1999 (1999-02), pages 252-258, XP002256112 figures 1,2	1-78
A	U RITZEL ET AL: "A synthetic glucagon-like peptide-1 analog with improved plasma stability" JOURNAL OF ENDOCRINOLOGY, vol. 159, 1998, pages 93-102, XP002256113 figures 3,4	1-78
	---	-/-

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>DORIS A. STOFFERS ET AL: "Insulinotropic Glucagon-Like Peptide 1 Agonists Stimulate Expression of Homeodomain Protein IDX-1 and Increase Islet Size in Mouse Pancreas"            DIABETES, vol. 49, May 2000 (2000-05), pages 741-748, XP002256114            figure 3</p> <p>---</p>	1-78
A	<p>US 6 344 180 B1 (HOLST J J ET AL)            5 February 2002 (2002-02-05)            claims 1-13</p> <p>-----</p>	1-78

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/DK 03/00463

## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 1-78 because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of Invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 1-78

Claims 1-78 relate to methods of treatment of the human or animal body by surgery or by therapy or diagnostic methods practiced on the human or animal body (PCT Rule 39.1(iv)).

The wording "drug holiday" is defined (Description, page 11, lines 29-30) as the time interval between a first endpoint (start) and a second endpoint (finish). Claim 1 seems to comprise such definition by the wording "...without the continuous presence of the molecule".

According to WO99/43708, the use of GLP-1 derivatives and exendin for the treatment of diabetes is known (See claim 89- WO99/43708). Therefore, the term "drug holiday" appears to be unclear if it referring to the dose administrated, in that case the claims 40-78 comprise also therapy or diagnostic methods practiced on the human or animal body (PCT Rule 39.1(iv)).

Consequently, a search has been carried out for on the alleged effects of the compounds or compositions for GLP-1 derivatives and exendin. Further, the search has covered the general aspects of the invention to some extent, although it lacks the necessary precision in the definition of the subject matter due to the large quantity of material known within GLP-1 and exendin derivatives.

The search for the general concept of GLP-1 derivatives and exendin will retrieve a pertinent document only if this concept is described in general terms in a reference. Specific solutions previously known and falling under the general concept - but failing to mention this fact - are likely not to be revealed in such a search.

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9943708	A	02-09-1999		AU 3247799 A WO 9943708 A1 EP 1056775 A1 JP 2003522099 T US 6268343 B1 US 2001011071 A1 US 2001047084 A1 ZA 9901571 A	15-09-1999 02-09-1999 06-12-2000 22-07-2003 31-07-2001 02-08-2001 29-11-2001 02-09-1999
-----					
WO 0132158	A	10-05-2001		US 2002177602 A1 AU 1082601 A AU 8022900 A BG 106732 A BG 106733 A BR 0015294 A BR 0015295 A CA 2389928 A1 CA 2389931 A1 CN 1414862 T CZ 20021547 A3 EP 1253944 A2 EP 1229918 A2 HU 0300218 A2 HU 0300642 A2 JP 20035119621 T LT 2002062 A ,B LT 2002063 A ,B NO 20022086 A NO 20022087 A SK 4992002 A3 WO 0132157 A2 WO 0132158 A2 US 2002183345 A1	28-11-2002 14-05-2001 14-05-2001 28-02-2003 28-02-2003 15-07-2003 24-06-2003 10-05-2001 10-05-2001 30-04-2003 15-01-2003 06-11-2002 14-08-2002 28-06-2003 28-07-2003 24-06-2003 25-03-2003 25-06-2003 24-06-2002 24-06-2002 01-04-2003 10-05-2001 10-05-2001 05-12-2002
-----					
US 6358924	B1	19-03-2002		AU 1617399 A CA 2312190 A1 EP 1049486 A1 JP 2001525371 T US 2002123466 A1 WO 9929336 A1	28-06-1999 17-06-1999 08-11-2000 11-12-2001 05-09-2002 17-06-1999
-----					
WO 0104156	A	18-01-2001		EP 1076066 A1 AT 242267 T AU 5966000 A CA 2378431 A1 CN 1376166 T DE 60003182 D1 WO 0184156 A1 EP 1196444 A1 EP 1329458 A2 JP 2003505347 T NZ 517012 A US 6528486 B1	14-02-2001 15-06-2003 30-01-2001 18-01-2001 23-10-2002 10-07-2003 18-01-2001 17-04-2002 23-07-2003 12-02-2003 28-02-2003 04-03-2003
-----					
EP 1329458	A	23-07-2003		EP 1196444 A1 EP 1076066 A1 EP 1329458 A2 AT 242267 T	17-04-2002 14-02-2001 23-07-2003 15-06-2003

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 1329458	A	AU 5966000 A CA 2378431 A1 CN 1376166 T DE 60003182 D1 WO 0104156 A1 JP 2003505347 T NZ 517012 A US 6528486 B1		30-01-2001 18-01-2001 23-10-2002 10-07-2003 18-01-2001 12-02-2003 28-02-2003 04-03-2003
US 6344180	B1 05-02-2002	AU 5489400 A CA 2376473 A1 EP 1185308 A2 JP 2003502344 T WO 0077039 A2 US 2003091507 A1		02-01-2001 21-12-2000 13-03-2002 21-01-2003 21-12-2000 15-05-2003